

AN INVESTIGATION INTO THE MECHANISM OF THE MENOPAUSAL HOT FLUSH

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Although menopausal hot flushes can be eliminated by oestrogens, the potential hazards of this therapy are well recognised. Furthermore, there is no evidence for a relation between circulating oestrogen levels and hot flushes. (Campbell 1976). The present study is an investigation of possible vasoactive factors involved in the hot flush which may lead to more specific therapy.

Six menopausal and four premenopausal women were studied at rest and during flushing and at rest and during warming respectively. Blood samples were taken from the antecubital vein into cold syringes, centrifuged at 2000 g at 4°C and the plasma stored at -18°C. All plasma samples were active on the rat fundic strip preparation with no consistent differences in potencies. Methysergide (10^{-7} M) caused a significantly greater reduction ($p < 0.01$) of responses to resting menopausal plasmas than to flushing plasmas, $26.7 \pm 4.1\%$ ($n = 16$) and $56.7 \pm 9.1\%$ ($n = 16$) respectively, of control. Premenopausal samples at rest and during warming were similarly reduced to $40 \pm 1.2\%$ ($n = 16$) and $42.3 \pm 4.1\%$ ($n = 16$) respectively.

This greater activity of flushing plasma related to resting plasma was investigated further. Hyoscine (10^{-7} M) reduced control acetylcholine (10^{-3} M) responses to $13.6 \pm 5.8\%$ ($n = 4$) but had little effect upon resting ($92.3 \pm 14.0\%$, $n = 4$) or flushing ($85.8 \pm 13.1\%$, $n = 4$) plasmas. Similarly mepyramine (5×10^{-5} M) reduced control histamine (10^{-6} M) responses to $24.0 \pm 7.2\%$ ($n = 4$) and responses to resting and flushing plasma to $94.1 \pm 14.2\%$ ($n = 4$) and $94.1 \pm 14.2\%$ ($n = 4$) and $94.0 \pm 13.8\%$ ($n = 4$) respectively. Neither resting nor flushing plasma contracted the guinea pig ileum. Both flushing and resting plasmas caused a non specific relaxation of rat duodenum which was unaffected by phentolamine (10^{-4} M) with propranolol (10^{-4} M) or by prior incubation with chymotrypsin (1.2×10^{-5} M). The absence of significant catecholamine-like activity was confirmed by the failure of either plasma to reduce contraction of rat ascending colon to potassium chloride and by the absence of pressor activity in the pithed rat preparation.

Whole blood prostaglandin E-like activity was determined by bioassay on the rat fundic strip following extraction (Greaves & MacDonald-Gibson, 1972). There was no significant difference between the levels at rest (10.5 ± 3.0 ng/ml, $n = 5$) and during flushing (12.2 ± 1.0 ng/ml, $n = 5$). Preliminary determination of bradykinin-like activity by bioassay on oestrus rat uterus following extraction from whole blood by the method of Mashford & Roberts (1972) showed no significant difference between the resting and flushing plasma levels in two patients.

The results indicate the presence of a vasoactive factor in the plasma which is absent at rest and which is not 5-hydroxytryptamine and which does not appear to be acetylcholine, catecholamines, histamine or prostaglandins.

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